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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,353	11/14/2003	Janine Schuurman	GMI-059	6363

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,353	SCHUURMAN ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-11,13,15,17,19-21,40-50,53-56,67 and 99-102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3, 5-11, 13, 15, 19-21, 55, 56, 67 and 99-102* is/are allowed.

6)☒ Claim(s) *2,4,40-50,53 and 54* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/4/07 and 8/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 2-11, 13, 15, 17, 19-21, 40-50, 53-56, 67 and 99-102 are all the pending claims for this application.

2. Claims 22-24, 28-30, 32-34, 36-39, 51, 52, 57-66, 69-89, 92-98 and 103-108 were cancelled, and Claims 2-11, 13, 15, 17, 19-21, 40, 43, 46, 49, 53-55 and 67 were amended in the Response of 8/21/07.

3. Claims 2-11, 13, 15, 17, 19-21, 40-50, 53-56, 67 and 99-102 are all the claims under examination.

4. Applicants amendment of the claims has raised new grounds for objection and rejection. This action is FINAL.

Information Disclosure Statement

5. The non-patent literature references cited in the IDS' of 6/4/07 and 8/21/07 have been considered and entered.

Withdrawal of Objections

Sequence Listing/New Matter

6. The objection to Applicant's request to enter a revised Sequence Listing of 2/8/07 in order to correct a "typographical error in SEQ ID NO:38" has been considered and entered. Applicants have identified the error in the sequence from the original Sequence Listing of 6/29/06 and where original support for the "corrected" sequence of SEQ ID NO:38 can be found in the application as filed.

Applicants' explanation on the top of p. 9 in the Response of 8/21/07 is duly noted.

Specification/New Matter

7. Applicant's request on p. 25, ¶1 of the Response of 2/8/07 to amend the specification to replace the Sequence Listing of 6/29/06 with the revised Sequence Listing has now been entered.

Applicants' explanation of the corrected Sequence Listing on the top of p. 9 in the Response of 8/21/07 is acknowledged.

Withdrawal of Rejections

Claim Rejections - 35 USC § 112, second paragraph

8. The rejection of Claims 2-11, 13, 15, 17, 19-21, 40-56 and 67 for the recitation "derived from...germline sequence" in Claims 51 and 52 is withdrawn and moot in view of Claims 51 and 52 having been cancelled.

Applicants' comments on p. 10 of the Response of 8/21/07 are acknowledged.

9. The rejection of Claims 2-11, 13, 15, 17, 19-21, 40-56 and 67 as being incomplete for omitting essential elements such as the transgenic mouse comprising the genetically inserted germline sequences of Claims 51 and 52 is withdrawn and moot in view of Claims 51 and 52 having been cancelled.

Applicants' comments on p. 10 of the Response of 8/21/07 are acknowledged.

10. The rejection of Claim 5 for reciting the broad recitation for a dissociation equilibrium constant (K_D) of "about 10^{-8} M or less", and the claim also recites "preferably of about 10^{-9} M or less" followed by "more preferably of about 10^{-10} M or less, or 10^{-11} M or even less", which is the narrower statement of the range/limitation, is withdrawn in view of amended Claim 5 to recite only a single range for the KD.

Applicants' comments on p. 10 of the Response of 8/21/07 are acknowledged.

Claims - 35 USC § 112, first paragraph

Written Description

11. The rejection of Claims 19 and 56 under 35 U.S.C. 112, first paragraph, for lack of written description support for the phrase where the variable domains are at least 90% homologous to the variable domains for the HC and LC of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14 and 16 is withdrawn. Applicants have amended Claim 19 to delete the phrase and their comments on the top of p. 10 of the Response of 8/21/07 are acknowledged.

Enablement

12. The rejection of Claims 2-11, 13, 15, 17, 19-24, 28-30, 32-34, 36-38, 40-56, and 67 under 35 U.S.C. 112, first paragraph, in lacking enablement for depending from Claims 51 and 52 (drawn to any human CD25 antibody having a VH derived from a human V_H1-69/JH4b or V_H1-69/JH5b germline sequence and VL derived from human A27/J_k4 or A27/J_k5 germline sequence (claim 51) and any human CD25 antibody having a VH derived from a human V_H1-69/D7-27/JH4b or V_H1-69/D7-27/JH5b germline

sequence and VL derived from human A27/J_k4 or A27/J_k5 germline sequence (claim 52)) is withdrawn and moot for cancelled claims 22-24, 28-30, 32-34 and 36-39 and further in view of Claims 51 and 52 being cancelled.

The rejection of Claims 103-108 under 35 U.S.C. 112, first paragraph, in lacking enablement for reciting that the CDR3 sequence comprises conservative sequence modifications is withdrawn and moot in view of the cancelled claims.

New Grounds for Objection

13. Claim 17 is objected to for the following informalities: Claim 17 should be amended to recite "which binds to human CD25," in order to be consistent with amended Claims 11, 13 and 15.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

14. Claims 2, 4, 40-50, 53 and 54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making fully human anti-CD25 (IL-2 receptor) monoclonal antibodies, AB7, AB12, AB1 or AB11, with the XenoMouse technology having a K_D of about 10^{-8} M or less, and using the antibodies to: inhibit

binding of IL-2 to CD25; inhibit anti-CD3 induced T cell proliferation of PBMCs; inhibit MLR; and internalize CD25 expressed on T cells, does not reasonably provide enablement for:

a) expressing the human anti-human CD25 antibody comprising the CDRs of AB7, AB12, AB1 or AB11 from a XenoMouse animal having the isotype of IgG2, IgG3, IgG4, IgM, IgA1, IgA2, secretory IgG, IgD or IgE;

b) making any conservative amino acid substitutions within CDRs of the AB7, AB12, AB1 or AB11 antibodies that do not remove antibody binding.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability of the art, the breadth of the claims, the quantity of experimentation which would be required in order to practice the invention as claimed.

The interpretation of Claims 2, 4, 40-50, 53 and 54 is of record. The claims have been amended to depend from any one of Claims 99-102.

a) The specification is not enabling for making or expressing any human anti-human CD25 antibody from a XenoMouse animal.

Claims 2, 4, 53 and 54 are directed to antibodies comprising the isotype of IgG2, IgG3, IgG4, IgM, IgA1, IgA2, secretory IgG, IgD or IgE. The same rejection was raised against these claims in the Office Action of 5/21/07.

Applicants have identified and characterized *only* four (4) anti-human CD25 antibody clones (AB1, AB7, AB11 and AB12) expressed from the germline gene sequence from HCo mice ((CMD)++; (HCo7) 11952+; (JKD) ++; (KCo5) 9272+ genotype) and ***all were IgG1, kappa*** (p. 56, lines 7-11).

As discussed in the Office Action of 5/21/07, Davis et al. ((1999) Can. Metastasis Rev. 18:421-425; cited in the PTO 892 form of 5/21/07) describes neutralizing antibodies for epidermal growth factor receptor produced from XenoMouse animals shared similar gene composition and out 8 clones each shared one of 2 VH genes (Table 3). Davis teaches "there appear to be rigorous structural requirements for antibodies that bind effectively to the ligand binding site on EGFr" (p. 425, Col. 1).

As discussed in the Office Action of 5/21/07, Gallo et al. (Eur. J. Immunol. (2000) 30:534-540; cited in the PTO form 892 of 5/21/07) compared XenoMouse and human VH gene segment usage for the VH3 and VH4 gene segments and found the same genes to utilized and to the same degree, thus the VH gene segmentation representation in the XenoMouse repertoire appears to be substantially the same as observed in humans (Figures 1 and 2). Similar findings were reported for JH gene segments between human and XenoMouse repertoires (Table 3).

Thus one skilled in the art could not have practiced or would have expected to obtain any Ig class of human anti-CD25 antibody having structural diversity from a

transgenic mouse and meeting all the functional properties for a human CD25 antibody as broadly encompassed by the claims.

b) The specification and the prior art are not enabling for making any conservative amino acid substitutions within CDRs that do not effect antibody binding.

Claims 40-50 are drawn to amino acid substituted VH CDR1 (Claim 40), VH CDR2 (Claim 43), VL CDR1 (Claim 46) and VL CDR3 (Claim 49) for any of the antibodies of claims 99-102. The same rejection was raised against Claims 40-50 in the Office Action of 5/21/07.

For purposes of brevity, the Examiner incorporates the arguments in full based in the cited references of record: Jang et al. (Molec. Immunol. 35:1207-1217 (1998)); Brorson et al. (J. Immunol. 163:6694-6701 (1999)); and Coleman (Research in Immunol. 145:33-36 (1994)).

It is unlikely that a human CD25 antibody having amino acid-modified CDRs, conservative or otherwise, from any one of monoclonal antibodies, AB7, AB12, AB1 or AB11, as defined by the claims would have the required binding function for human CD25 absent a showing to the contrary. The specification provides no examples of the genus of antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Conclusion

15. Claims 3, 5-11, 13, 15, 19-21, 55, 56, 67 and 99-102 appear to be free of prior art and in condition for allowance.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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